

CLAIM AMENDMENTS

IN THE CLAIMS

This listing of the claims will replace all prior versions, and listing, of claims in the application or previous response to office action:

1. (Currently Amended) A unicellular organism for producing a diterpene, comprising:

~~an~~ a first exogenous nucleic acid having the sequence of SEQ ID NO: 1 and encoding a geranylgeranyl pyrophosphate synthase, the first nucleic acid under the control of a first promoter operable in said organism; and

~~an~~ a second exogenous nucleic acid having the sequence of SEQ ID NO: 361 and encoding a diterpene synthase, the second nucleic acid under the control of a second promoter operable in said organism.

2-3. (Cancelled).

4. (Currently Amended) The unicellular organism of claim 1, wherein said first promoter ~~of said nucleic acid sequence encoding said geranylgeranyl pyrophosphate synthase is comprises~~ an inducible promoter or a constitutive promoter.

5. (original) The unicellular organism of claim 4, wherein said inducible promoter is selected from the group consisting of GAL1, CUP1 and MET3.

6. (Currently Amended) The unicellular organism of claim 4, wherein said constitutive promoter is selected from the group consisting of ADH and PGK alcohol dehydrogenase (ADH) promoter and phosphoglycerine kinase (PGK) promoter.

7. (Currently Amended) The unicellular organism of claim 1, wherein said ~~second promoter of said nucleic acid sequence encoding said diterpene synthase is~~ comprises an inducible promoter or a constitutive promoter.

8. (original) The unicellular organism of claim 7, wherein said inducible promoter is selected from the group consisting of GAL1, CUP1 and MET3.

9. (Currently Amended) The unicellular organism of claim 7, wherein said constitutive promoter is selected from the group consisting of ~~ADH and PGK~~ alcohol dehydrogenase (ADH) promoter and phosphoglycerine kinase (PGK) promoter.

10. (Currently Amended) The unicellular organism of claim 1, wherein said unicellular organism further comprises ~~an~~ a third exogenous nucleic acid ~~sequence~~ encoding a soluble form of ~~an HMG-a 3-hydroxy-3-methylglutaryl~~-CoA reductase under control of a third promoter operable in said organism.

11. (Currently Amended) The unicellular organism of claim 10, wherein said third promoter ~~is~~ comprises an inducible promoter or a constitutive promoter.

12. (original) The unicellular organism of claim 11, wherein said inducible promoter is selected from the group consisting of GAL1, CUP1 and MET3.

13. (Currently Amended) The unicellular organism of claim 11, wherein said constitutive promoter is selected from the group consisting of ~~ADH and PGK~~ alcohol dehydrogenase (ADH) promoter and phosphoglycerine kinase (PGK) promoter.

14. (Currently Amended) The unicellular organism of claim 10, wherein said unicellular organism further comprises ~~an~~ a fourth exogenous nucleic acid having the sequence of SEQ ID NO: 399 under control of a fourth promoter operable in said

~~organism that confers to said organism an increase in sterol metabolic flux as compared to native sterol metabolic flux levels.~~

15. (Currently Amended) The unicellular organism of claim 1, wherein said first nucleic acid ~~sequence~~ encoding said geranylgeranyl pyrophosphate synthase is present on a chromosome of said unicellular organism.

16. (original) The unicellular organism of claim 1, wherein said unicellular organism is a yeast.

17. (original) The unicellular organism of claim 10, wherein said unicellular organism is a yeast.

18. (original) The unicellular organism of claim 14, wherein said unicellular organism is a yeast.

19-28. (Cancelled).

29. (Currently Amended) A unicellular organism for producing a diterpene or diterpene precursor, comprising:

~~an a first~~ exogenous polynucleotide ~~sequence~~ encoding a polypeptide having an amino acid sequence of SEQ ID NO: 22 of a geranylgeranyl pyrophosphate synthase, the first polynucleotide under the control of a first promoter operable in said organism; and

~~an a second~~ exogenous polynucleotide ~~sequence~~ encoding a polypeptide having an amino acid sequence of SEQ ID NO: 383 of a diterpene synthase, the second polynucleotide under the control of a second promoter operable in said organism;

~~an exogenous polynucleotide sequence encoding a polypeptide having an amino acid sequence of a soluble form of HMG-CoA reductase under control of a promoter operable in said organism; and~~

~~an exogenous polynucleotide sequence encoding a polypeptide having an amino acid sequence of gene that confers to said organism an increase in sterol metabolic flux as compared to native sterol metabolic flux levels.~~

30-31. (Cancelled).

32. (original) The unicellular organism of claim 29, wherein said organism is a yeast.

33-79. (Cancelled).

80. (New) The unicellular organism of claim 10, wherein said unicellular organism further comprises a fourth exogenous nucleic acid encoding a upc2-1 allele under control of a fourth promoter operable in said organism.

81. (New) The unicellular organism of claim 29, wherein said first promoter comprises an inducible promoter or a constitutive promoter.

82. (New) The unicellular organism of claim 81, wherein said inducible promoter is selected from the group consisting of GAL1, CUP1 and MET3.

83. (New) The unicellular organism of claim 81, wherein said constitutive promoter is selected from the group consisting of alcohol dehydrogenase (ADH) promoter and phosphoglycerine kinase (PGK) promoter .

84. (New) The unicellular organism of claim 29, wherein said second promoter comprises an inducible promoter or a constitutive promoter.

85. (New) The unicellular organism of claim 84, wherein said inducible promoter is selected from the group consisting of GAL1, CUP1 and MET3.

86. (New) The unicellular organism of claim 84, wherein said constitutive promoter is selected from the group consisting of alcohol dehydrogenase (ADH) promoter and phosphoglycerine kinase (PGK) promoter .

87. (New) The unicellular organism of claim 29, wherein said unicellular organism further comprises a third exogenous polynucleotide encoding a soluble form of 3-hydroxy-3-methylglutaryl-CoA reductase under control of a third promoter operable in said organism.

88. (New) The unicellular organism of claim 87, wherein said third promoter comprises an inducible promoter or a constitutive promoter.

89. (New) The unicellular organism of claim 88, wherein said inducible promoter is selected from the group consisting of GAL1, CUP1 and MET3.

90. (New) The unicellular organism of claim 88, wherein said constitutive promoter is selected from the group consisting of alcohol dehydrogenase (ADH) promoter and phosphoglycerine kinase (PGK) promoter .

91. (New) The unicellular organism of claim 87, wherein said unicellular organism further comprises a fourth exogenous polynucleotide having the sequence of SEQ ID NO: 399 and under control of a fourth promoter operable in said organism.

92. (New) The unicellular organism of claim 87, wherein said unicellular organism further comprises an exogenous polynucleotide encoding a upc2-1 allele and under control of a fourth promoter operable in said organism.

93. (New) The unicellular organism of claim 29, wherein said first polynucleotide encoding said geranylgeranyl pyrophosphate synthase is present on a chromosome of said unicellular organism.

94. (New) The unicellular organism of claim 87, wherein said unicellular organism is a yeast.

95. (New) The unicellular organism of claim 80, wherein said unicellular organism is a yeast.

96. (New) The unicellular organism of claim 91, wherein said unicellular organism is a yeast.

97. (New) The unicellular organism of claim 92, wherein said unicellular organism is a yeast.

98. (New) The unicellular organism of claim 14, wherein said fourth nucleic acid and promoter are operable to confer to said organism an increase in sterol metabolic flux as compared to native sterol metabolic flux levels.

99. (New) The unicellular organism of claim 80, wherein said fourth nucleic acid and promoter are operable to confer to said organism an increase in sterol metabolic flux as compared to native sterol metabolic flux levels.

100. (New) The unicellular organism of claim 91, wherein said fourth nucleic acid and promoter are operable to confer to said organism an increase in sterol metabolic flux as compared to native sterol metabolic flux levels.

101. (New) The unicellular organism of claim 92, wherein said fourth nucleic acid and promoter are operable to confer to said organism an increase in sterol metabolic flux as compared to native sterol metabolic flux levels.

102. (New) The unicellular organism of Claim 1, further comprising a vector having the first exogenous nucleic acid and first promoter.

103. (New) The unicellular organism of Claim 1, further comprising a vector having the second exogenous nucleic acid and second promoter.

104. (New) The unicellular organism of Claim 10, further comprising a vector having the third exogenous nucleic acid and third promoter.

105. (New) The unicellular organism of Claim 14, further comprising a vector having the fourth exogenous nucleic acid and fourth promoter.

106. (New) The unicellular organism of Claim 80, further comprising a vector having the fourth exogenous nucleic acid and fourth promoter.

107. (New) The unicellular organism of Claim 29, further comprising a vector having the first exogenous polynucleotide and first promoter.

108. (New) The unicellular organism of Claim 29, further comprising a vector having the second exogenous polynucleotide and second promoter.

109. (New) The unicellular organism of Claim 87, further comprising a vector having the third exogenous polynucleotide and third promoter.

110. (New) The unicellular organism of Claim 91, further comprising a vector having the fourth exogenous polynucleotide and fourth promoter.

111. (New) The unicellular organism of Claim 92, further comprising a vector having the fourth exogenous polynucleotide and fourth promoter.

112. (New) The unicellular organism of Claim 1, further comprising a first enhancer operable to enhance transcriptional activation of the first nucleic acid.

113. (New) The unicellular organism of Claim 1, further comprising a second enhancer operable to enhance transcriptional activation of the second nucleic acid.

114. (New) The unicellular organism of Claim 1, further comprising a third enhancer operable to enhance transcriptional activation of the third nucleic acid.

115. (New) The unicellular organism of Claim 1, further comprising a fourth enhancer operable to enhance transcriptional activation of the fourth nucleic acid.

116. (New) The unicellular organism of Claim 1, further comprising a fourth enhancer operable to enhance transcriptional activation of the fourth nucleic acid.

117. (New) The unicellular organism of Claim 1, further comprising a first enhancer operable to enhance transcriptional activation of the first polynucleotide.

118. (New) The unicellular organism of Claim 1, further comprising a second enhancer operable to enhance transcriptional activation of the second polynucleotide.

119. (New) The unicellular organism of Claim 1, further comprising a third enhancer operable to enhance transcriptional activation of the third polynucleotide.

120. (New) The unicellular organism of Claim 1, further comprising a fourth enhancer operable to enhance transcriptional activation of the fourth polynucleotide.

121. (New) The unicellular organism of Claim 1, further comprising a fourth enhancer operable to enhance transcriptional activation of the fourth polynucleotide

122. (New) The multicellular organism of Claim 1, wherein the first and second promoters are the same promoter.

123. (New) The multicellular organism of Claim 10, wherein at least two of the first, second and third promoters are the same promoter.

124. (New) The multicellular organism of Claim 14, wherein at least two of the first, second, third and fourth promoters are the same promoter.

125. (New) The multicellular organism of Claim 80, wherein at least two of the first, second, third and fourth promoters are the same promoter.

126. (New) The multicellular organism of Claim 29, wherein the first and second promoters are the same promoter.

127. (New) The multicellular organism of Claim 87, wherein at least two of the first, second and third promoters are the same promoter.

128. (New) The multicellular organism of Claim 91, wherein at least two of the first, second, third and fourth promoters are the same promoter.

129. (New) The multicellular organism of Claim 92, wherein at least two of the first, second, third and fourth promoters are the same promoter.

130. (New) The multicellular organism of Claim 1, wherein at least one exogenous nucleic acid comprises an ATG translation initiation codon located 5' to a coding region and in-frame with the coding region.

131. (New) The multicellular organism of Claim 29, wherein at least one exogenous nucleic acid comprises an ATG translation initiation codon located 5' to a coding region and in-frame with the coding region.

132. (New) The multicellular organism of Claim 1, wherein a single exogenous nucleic acid comprises both the first and second exogenous nucleic acids.

133. (New) The multicellular organism of Claim 1, wherein the single exogenous nucleic acid comprises at least one internal ribosome binding site.

134. (New) The multicellular organism of Claim 29, wherein a single exogenous polynucleotide comprises both the first and second exogenous polynucleotides.

135. (New) The multicellular organism of Claim 1, wherein the single exogenous polynucleotide comprises at least one internal ribosome binding site.

136. (New) A unicellular organism for producing a diterpene, comprising:
a first exogenous nucleic acid having the sequence of SEQ ID NO: 1 and encoding a geranylgeranyl pyrophosphate synthase having the amino acid sequence of SEQ ID NO: 22, the first nucleic acid under the control of a first promoter operable in said organism; and
a second exogenous nucleic acid having the sequence of SEQ ID NO: 361 and encoding a diterpene synthase having the amino acid sequence of SEQ ID NO: 383, the second nucleic acid under the control of a second promoter operable in said organism.

137. (New) The unicellular organism of Claim 136, wherein the unicellular organism is a yeast.

138. (New) A unicellular organism for producing a diterpene, comprising:

a first exogenous nucleic acid having the sequence of SEQ ID NO: 1 and encoding a geranylgeranyl pyrophosphate synthase having the amino acid sequence of SEQ ID NO: 22, the first nucleic acid under the control of a first promoter operable in said organism;

a second exogenous nucleic acid having the sequence of SEQ ID NO: 361 and encoding a diterpene synthase having the amino acid sequence of SEQ ID NO: 383, the second nucleic acid under the control of a second promoter operable in said organism; and

a third exogenous nucleic acid encoding a soluble form of 3-hydroxy-3-methylglutaryl-CoA reductase, the third nucleic acid under control of a third promoter operable in said organism.

139. (New) The unicellular organism of Claim 138, wherein the unicellular organism is a yeast.

140. (New) A unicellular organism for producing a diterpene, comprising:

a first exogenous nucleic acid having the sequence of SEQ ID NO: 1 and encoding a geranylgeranyl pyrophosphate synthase having the amino acid sequence of SEQ ID NO: 22, the first nucleic acid under the control of a first promoter operable in said organism;

a second exogenous nucleic acid having the sequence of SEQ ID NO: 361 and encoding a diterpene synthase having the amino acid sequence of SEQ ID NO: 383, the second nucleic acid under the control of a second promoter operable in said organism;

a third exogenous nucleic acid encoding a soluble form of 3-hydroxy-3-methylglutaryl-CoA reductase, the third nucleic acid under control of a third promoter operable in said organism; and

a fourth exogenous nucleic acid having the sequence of SEQ ID NO: 399 and encoding a upc2-1 allele, the fourth nucleic acid under control of a fourth promoter operable in said organism.

141. (New) The unicellular organism of Claim 140, wherein the unicellular organism is a yeast.